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- a first portion of said plurality of nucleotides have B-form conformational geometry and are joined together in a continuous sequence, at least two of said nucleotides of said first portion being ribonucleotides; and
- a further portion of said plurality of nucleotides are ribonucleotide that have A-form conformation geometry and are joined together in at least one continuous sequence.

4 (Amended). The oligonucleotide of claim 1 wherein each nucleotide of said further portion, independently, is a 2'-fluoro nucleotide or a nucleotide having a 2'-substituent having the formula I or II:

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PATENT

$$-O - \left( (CH_2)_{q1} - O - N - Q_1 \right)_{q2} - O - E - CH_2 - Q_1 - O - E - CH_2 - Q_1 - Q_2 - Q_1 - Q_2 - Q_$$

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wherein

E is  $C_1$ - $C_{10}$  alkyl,  $N(Q_1)(Q_2)$  or  $N=C(Q_1)(Q_2)$ ;

each  $Q_1$  and  $Q_2$  is, independently, H,  $C_1$ - $C_{10}$  alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support, or  $Q_1$  and  $Q_2$ , together, are joined in a nitrogen protecting group or a ring structure optionally containing at least one additional heteroatom selected from N and O;

 $R_3$  is OX, SX, or  $N(X)_2$ ;

each X is, independently, H,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  haloalkyl, C(=NH)N(H)Z, C(=O)N(H)Z or OC(=O)N(H)Z;

Z is H or  $C_1$ - $C_8$  alkyl;

 $L_1$ ,  $L_2$  and  $L_3$  form a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;